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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/997,240	11/30/2001	Wen Liang Yan	0249-0001	2508
32256	7590	12/28/2005	EXAMINER	
REED SMITH LLP 1301 K STREET, N.W. SUITE 1100 EAST TOWER WASHINGTON, DC 20005			WOITACH, JOSEPH T	
			ART UNIT	PAPER NUMBER
			1632	

DATE MAILED: 12/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.	Applicant(s)	
09/997,240	YAN ET AL.	
Examiner	Art Unit	
Joseph T. Voitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 05 October 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 2-4, 7-82 and 84-91 is/are pending in the application.
- 4a) Of the above claim(s) 7-69, 74, 76-79, 81 and 85-88 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2-4, 70-73, 75, 80, 82-84 and 89-91 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 November 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 10, 2005 has been entered.

**DETAILED ACTION**

This application claims benefit to provisional application 60/253943, filed November 30, 2000.

Applicants' amendment filed October 10, 2005, has been received and entered. Claims 1, 5, 6 and 83 have been canceled. Claims 2-4, 70-73, 75, 80, 82, 84 and 89-91 have been amended. Claims 2-4, 7-82, 84-91 are pending.

***Election/Restriction***

Applicant's election without traverse of Group I, in the reply filed on March 30, 2004 was acknowledged. No arguments have been provided in the instant amendment.

Claims 2-4, 7-82, 84-91 are pending. Claims 7-69, 74, 76-79, 81, 85-88 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Claims 2-4, 70-73, 75, 80, 82-84, 89-91 drawn to an isolated homozygous stem cell, are currently under examination.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-4, 70-73, 75, 80, 82, 84, 89-91 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application". Specifically, the amendment to the claims to encompass a "chromosomally homozygous stem cell" is considered new matter. A search of the instant specification for the literal support of the term "chromosomally" does not identify any support for the term. In a review for figurative support, the only support for such a structural limitation would derive from the methods used to obtain a "homozygous stem cell" (recited and supported in the instant specification). In this case, the methodology used, parthenogenetically activating an oocyte and generating a cell would result in all the genetic material to be maternal in origin, but would not

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result in homozygous (*i.e.* identical) pairs of chromosomes. The methodology used for parthenogenesis was known prior to the time of filing, and would not exclude inherent features of meiosis, such as chromosomal exchange resulting in unique chromosome pairs, nor the fact that in generating a parthenogenetic cell there is no control over the exchange of genetic material nor what chromosomes are ultimately maintained by the resulting cell. In any case, in meiosis there is no duplication of one chromosome resulting in two identical or homozygous chromosomes that are segregated during meiosis, thus would not provide for a cell derived from an oocyte that would have such a feature.

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, claims 2-4, 70-73, 75, 80, 82, 84, 89-91 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described. As discussed above, the methodology of parthenogenesis is not novel, and since the methods require such methods, any feature inherent to those methods would also be inherent to the instantly claimed methods. Since the methodology provides no control over genetic recombination, nor the ability to control which chromosome pairs ultimately end up in the resulting cell, there is no reasonable expectation of success based on the guidance of the present specification. Similar methodology in generating stem cells has been reported in the post filing art, however Cibelli *et al.* clearly indicate that the resulting cells are not homozygous, rather considered “autologous” to the oocyte (page 819, second column), and Vrana *et al.* teach that the resulting cells appear “to be similar to traditional

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ES cells, it is reasonable to question their viability and utility” (page 11916, first column) since they are derived from only maternal DNA and that imprinting may affect the “Stemness” of the resulting cell (page 11916, second column) when evaluated and compared to other characterized stem cells in the art.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure".

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-4, 70-73, 75, 80, 82, 84, 89-91 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the claims have been amended to

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recite “chromosomally homozygous”, and review of the present specification fails to provide a specific definition of this terminology. The metes and bounds of the term and the claim are unclear and indefinite because what is being compared chromosomally and considered homozygous is not clearly set forth in the claim nor the specification. It is unclear in evaluating the breadth of the claims whether it is portions of the chromosomes that are to be homozygous, or that the cells simply have the same complement of number of chromosomes compared to one another (thus, all male or female human cells are homozygous to one another). The terminology in the present claims is not defined in the specification, nor is an art accepted term, except at best when referring to a specific allele of a cell, not in the context of a whole chromosome. Even considering the methods encompassed by the product by process claims, it is unclear whether a single base pair alteration in one chromosome as compared to another in a resulting cell would or would not be encompassed by the instant claims since the pair of chromosomes would not be identical or homozygous to each other.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2, 70-73, 75, 80, 82-84 stand rejected and newly added claims 89-91 are rejected under 35 U.S.C. 102(b) as being anticipated by Thomson *et al.* (Science 1998-IDS reference).

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Claims 2-4, 70-73, 75, 80, 82-84 stand rejected and newly added claims 89-91 are rejected under 35 U.S.C. 102(b) as being anticipated by Doetschman *et al.* (J. Embryol. Exp. Morph 1985-IDS reference).

Claims 2-4, 70-73, 75, 80, 82-84 stand rejected and newly added claims 89-91 are rejected under 35 U.S.C. 102(b) as being anticipated by Evans *et al.* (Nature 1981-IDS reference).

Claims 2-4, 70-73, 75, 80, 82-84 stand rejected and newly added claims 89-91 are rejected under 35 U.S.C. 102(b) as being anticipated by Saito *et al.* (Dev. Biol. 1992-IDS reference).

Applicants provide a explanation of the present invention noting that chromosomes may be homozygous at single alleles but not over the entire chromosome as it would be in the instantly claimed cells (pages 14-15). For each of Thomson *et al.*, Doetschman *et al.*, Evans *et al.* and Saito *et al.* Applicants summarizing the stem cell described in each of the references, and argue that the methods used by the references would not provide the homozygosity of the described cell. Applicants arguments have been fully considered, but not found persuasive.

The claims under examination are generally drawn to an isolated homozygous stem cell, are currently under examination, while claims 5, 6, 70-73, 75, 80 and 82-84 are produced by particular methods. The issue is whether the methods disclosed in the instant specification result in a stem cell that is materially different from that in the cited art. Initially, it is noted that the specification provides a definition of a "homozygous stem cell" as a cell previously termed a teratoma stem cell or a cell made by a variety of methods, including the isolation of stem cells as the cells isolated from the inner cell mass of blastocyst-like masses (see bottom of page 16).



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Newly added claims 89-91 set forth three parameters of homozygous as in haplotypes, alleles and units of genetic material. Initially, given the definition provided in the instant specification or even a comparison of parameters such as haplotype, allele, stem cells obtained from an individual or from a embryo made by IVF would have common haplotype, alleles or genetic units. A unit of genetic material is a very broad term and could reasonably be interpreted to be any genetic sequence. It appear that Applicants are attempting to define the term of homozygosity to be identical pairs of chromosomes, however even their methodology would not produce such a cell. During meiosis, recombination occurs between chromosomes such that each of the resulting germ cell is different from one another. Thus, even the product by process claims were two germ cells are recombined back into one cell, the method would result in a cell that indistinguishable from those in the cited art. Applicants have simply argued that the cited references do not teach that the stem cells are homozygous without providing any clear scientific basis for why the claimed cell can be distinguished from these stem cells.

As noted previously, where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See *In re Ludtke* 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, or "*prima facie obviousness*" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

As noted previously, Thomson *et al.* teach the isolation and characterization of human embryonic stem cells, Doetschman *et al.* teach the isolation and characterization of mouse embryonic stem cells, Evans *et al.* teach the isolation and characterization of mouse embryonic stem cells, and Saito *et al.* teach the isolation and characterization of bovine embryonic stem cells.

For the reasons above and of record, the rejections are maintained.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 2-4, 70-73, 75, 80, 82-84 rejected and newly added claims 89-91 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5, 7-14 of copending Application No. 10/179959 is withdrawn.

Applicants terminal disclaimer has been accepted.

Claims 2-4, 70-73, 75, 80, 82, 84, 89-91 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 29, 32 and 33 of copending Application No. 10/032,495 (filed January 2, 2002). Although the conflicting claims are not identical, they are not patentably distinct from each other because practicing the methods of '495 would result in the cells instantly claimed, each encompassing the generation of embryonic stem cells wherein parthenogenesis is used to generate the embryo from which the cells are obtained. The methods of '495 indicate that the MHC is characterized for each of the resulting cells, however the MHC haplotype is present in all resulting cells and would be an inherent feature of the presently claimed cells if characterized or not. The instant claims encompass the breadth of products produced by the methods of '495.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented. However, it is noted that a notice of Allowance has been mailed in '495, and the rejection will be made non-provisional upon issuance.

### ***Conclusion***

No claim is allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Voitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached at (571) 272-0735.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Voitach

*Joe Voitach*  
*AVK32*